

What is claimed is:

1. An isolated nucleic acid molecule encoding APEX-1.
- 5 2. The isolated nucleic acid molecule of claim 1, wherein the molecule begins with a guanine (g) at position 1 and ends with an adenine (a) at position 2704 as shown in SEQ ID NO. 1.
3. The isolated nucleic acid molecule of claim 1, wherein APEX-1 has an amino
10 acid sequence shown in SEQ ID NO. 4.
4. The isolated nucleic acid molecule of claim 3, wherein the amino acid sequence is
15 encoded by a nucleotide sequence beginning with adenine (a) at position 42 and ending with guanine (g) at position 1049 as shown in SEQ ID NO. 1.
5. The isolated nucleic acid molecule of claim 1, wherein APEX-1 has an
20 extracellular domain encoded by nucleotide sequences beginning with thymine (t) at position 108 and ending with cytosine (c) at position 716 as shown in SEQ ID NO. 1.
6. An isolated nucleic acid molecule encoding APEX-2.
7. The isolated nucleic acid molecule of claim 6, wherein the molecule begins with
25 thymine (t) at position 1 and ends with thymine (t) at position 1516 as shown in SEQ ID NO.2, or a fragment thereof.
8. The isolated nucleic acid molecule of claim 6, wherein APEX-2 has an amino
acid sequence shown in SEQ ID NO. 5.
- 30 9. The isolated nucleic acid molecule of claim 8, wherein the amino acid sequence is encoded by a nucleotide sequence beginning with adenine (a) at position 162 and ending with adenine at position 1217 as shown in SEQ ID NO. 2.

10. The isolated nucleic acid molecule of claim 6, wherein APEX-2 has an extracellular domain encoded by nucleotide sequences beginning at adenine (a) at position 249 and ending with guanine (g) at position 875 as shown in SEQ ID NO. 2.

11. An isolated nucleic acid molecule encoding APEX-3.

12. The isolated nucleic acid molecule of claim 11, wherein the molecule begins with guanine (g) at position 1 and ends with guanine (g) at position 1408 as shown in SEQ ID NO. 3.

13. The isolated nucleic acid molecule of claim 11, wherein APEX-3 has an amino acid sequence shown in SEQ ID NO. 6.

14. The isolated nucleic acid molecule of claim 13, wherein the amino acid sequence is encoded by a nucleotide sequence beginning with adenine (a) at position 115 and ending with adenine at position 972 as shown in SEQ ID NO. 3.

15. An isolated polynucleotide variant having at least 70% polynucleotide sequence identity to the polynucleotide of claim 1, 6, or 11.

16. An isolated polynucleotide which hybridizes under stringent conditions to the complement of polynucleotide of claim 1, 6, or 11.

17. An isolated nucleic acid molecule comprising a nucleotide sequence which is complementary to the isolated nucleic acid molecule of claim 1, 6, or 11.

18. The isolated nucleic acid molecule of claim 1, 6, or 11 which is DNA or RNA.

19. The isolated nucleic acid molecule of claim 18, wherein the DNA is cDNA.

20. The isolated nucleic acid of claim 18, wherein the RNA is mRNA.

21. The isolated nucleic acid molecule of claim 1, 6, or 11 which is labeled with a detectable marker.

22. The nucleic acid molecule of claim 21, wherein the detectable marker is selected from the group consisting of a radioisotope, a fluorescent compound, a bioluminescent compound, a chemiluminescent compound, a metal chelator and an enzyme.

23. A vector comprising the nucleotide sequence of claim 1, 6, or 11.

24. A host vector system comprising the vector of claim 23 in a suitable host cell.

25. The host vector system of claim 24, wherein the suitable host is a bacterial cell.

26. The host vector system of claim 24, wherein the suitable host is an eukaryotic cell.

27. An isolated protein designated APEX-1 or APEX-2, comprising an extracellular domain having at least one Ig-like structure and at least one N-glycosylation site, a transmembrane domain, and a cytoplasmic domain having at least one SH2-binding motif.

28. The isolated protein designated APEX-1 of claim 27, having the amino acid sequence beginning at Met at position 1 and ending at Ile at position 335 as shown in SEQ. ID. No. 4, or fragments thereof, the protein or the fragments having APEX activity.

29. The isolated protein designated APEX-2 of claim 27, having the amino acid sequence beginning with Met at position 1 and ending at Ser at position 351 as shown in SEQ. ID. NO. 5, or fragments thereof, the protein or the fragments having APEX activity.

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30. An isolated protein designated APEX-3 consisting of the amino acid sequence beginning with Met at position 1 and ending at Pro at position 285 as shown in SEQ. ID. NO. 6.

10 31. An antibody which recognizes and binds to the isolated protein of claim 27 or 30, or a fragment thereof having APEX activity.

32. A Fab', F(ab)2', or Fv fragment of the antibody of claim 31.

15 33. The antibody of claim 31, which is a monoclonal antibody.

34. The antibody of claim 33, which is 40-A10-G3 (ATCC Accession No.).

35. The antibody of claim 33, which is 66-H2-E5 (ATCC Accession No.).

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36. The antibody of claim 33, which is 68-F12-G6 (ATCC Accession No.).

37. The antibody of claim 33, which is 71-E9-F10 (ATCC Accession No.).

25 38. The antibody of claim 31, which is a polyclonal antibody.

39. The antibody of claim 31, wherein the antibody is a chimeric antibody having a murine antigen-binding site and a humanized region that regulates effector functions.

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40. The antibody of claim 31 which is labeled with a detectable marker.

41. The antibody of claim 40, wherein the detectable marker is selected from the group consisting of a radioisotope, a fluorescent compound, a bioluminescent compound, a chemiluminescent compound, a metal chelator and an enzyme.

5 42. A method of producing an APEX protein comprising:
a) culturing the host-vector system of claim 24 under suitable conditions so as to produce the APEX protein; and
b) recovering the APEX protein so produced.

10 43. An APEX protein produced by the method of claim 42.

44. A soluble APEX protein having a first amino acid sequence corresponding to an extracellular domain of an APEX protein and a second amino acid sequence corresponding to a moiety that alters the solubility of said APEX protein.

15 45. The soluble APEX protein of claim 44, wherein said moiety is an immunoglobulin constant region.

20 46. The soluble APEX protein of claim 44, wherein the APEX protein is APEX-1, APEX-2, or APEX-3.

47. A method for identifying a molecule in a sample which specifically binds an APEX protein, the method comprising:

25 (a) contacting the APEX protein with the sample under suitable conditions so as to obtain a complex having the APEX protein and the molecule;

(b) recovering the complex; and

30 (c) separating the APEX protein from the molecule in the complex and identifying the molecule so separated.

48. A method of of claim 47, wherein the sample is a tissue, e.g., brain, bone marrow, heart, kidney, liver, lung, lymph node, pancreas, placenta, skeletal muscle, thymus.

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49. A method of claim 47, wherein the sample is a biological fluid, e.g., blood, urine, plasma, serum.

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50. A nucleic acid molecule having a nucleotide sequence selected from a group consisting of SEQ ID NO: 7 to SEQ ID NO: 42.

51. A pharmaceutical composition comprising the APEX protein of claim 28, 29, or 30, and an acceptable carrier.

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52. A pharmaceutical composition comprising an antibody or a antibody fragment thereof, that recognizes an APEX protein, and an acceptable carrier.

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